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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

ON LUNG DEPOSITS, THROUGH BREATHING, OF SMALL PARTICLES SUSPENDED IN THE AIR

By W. Findeisen, Munich

(entered 27 June 1935)

Trans. by B.R. Robins

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On lung deposits, through breathing, of small particles suspended in the air.[1]

by W. Findeisen, Munich
with 8 illustrations

(entered 27 June 1935)

The following work, by means of lengthy calculations based on schematised hypotheses, give the aerosol (smoke, fog) particle percentage filtered out during passage through the human lung at various stages of the bronchial tree. The filtering stems from the fact that the particles are subjected to four forces, th be discussed later, until deposited on the walls of the bronchi and bronchioli and alveoli attached there. The aim of the calculations discussed here is to solve the problem of lung inhalation, if only superficially, at least on a quantitatively basis. On the basis of the calculation results, one should be able to discover what size aerosol particles must be so as to be intentionally deposited in large numbers at certain places in the lungs and there to be set to work. This question could be of great medical importance.

1. Plan of the bronchial tree and of breathing

So as to be able to handle quantitatively, the flowing process, which take place in the human lung because of respiration, it is necessary to adopt a simplified plan of the bronchial tree. The plan is presented in table I (The scalar numbers are partly taken from Sieglbauer)

The seperate parts of the bronchial tree will here be labeled with letters A,B,C, etc. It is assumed that the bronchi and bronchioli are cylindrical tubes, whereas the alveolar sacculi are spheres; further, that the bronchi and bronchioli in the same manner are at equal distance and of equal length. Supplementary, simplifying suppositions will be made later, on the bifurcations and forking places of bronchi and bronchioli. As the rapidity of the in the lung tract must be given for the calculations, the respiratory curve shown in Figure 1, which reflects quiet deep breathing, will be adopted. The schematic data results in the stream velocities and "Through Stream Timing" in sectional parts of the lungs as presented in Table I.

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[1] Note: I became interested in this work during my activity as physicist at the Institute for Air Travel Medicine and Climactic research in Hamburg (Eppendorfer Hospital) during the years 1931-32. For the suggestions and the medical advice I first thank the Director, Prof. Dr. L. Brauer, and Dr. Zeplin.

Table 1. Plan of the bronchial tree.

Lung Sections	Splitting Factor	Count	Internal measurement	Total cross section	Distance vel.	Streaming through time	Length
A Trachea	1	1	1.2	1.3	150	0.07	11.0
B Mainbronchi	2	2	0.75	1.1	140	0.04	6.5
C Bronchi 1. order	6	12	014	1.5	130	0.02	3.0
D " 2. "	8	100	0.2	3.1	65	0.02	1.5
E " 3. "	8	770	0.15	14	14	0.04	0.5
F Bronchioli terminales	70	$5.4x10^4$	0.06	150	1.3	0.22	0.3
G Bronchioli respiratorii	2	$1.1x10^5$	0.05	200	0.9	017	0.15
H Ductuli alveolarii	240	$2.6x10^7$	0.02	6300	0.025	0.32	0.02
I Sacculi alveolarii	2	$5.3x10^7$	0.03	(147000)**	0	1.2	0.03

* For 200 ccm/sec ventilation velocity

** Total surface of the spherical sacculi alveolarii

It is assumed that the stream velocities are always equal in the entire tube cross section, on the basis of mathematical simplification. This fact is indeed never actually fulfilled, but it can really falsify the conclusions arrived at below; the final values will only be a little too high.

The particles suspended in the air are brought into contact with the walls of the lung through four processes independent of one another. As is known from similar processes, every contact of a particle with the moist walls (mucous membrane) results in the particles becoming stuck. The four processes discussed below establish the reasons for deposits of particles in the lung syste.

2. The processes which cause deposits of particles in the lung system

a) Brownian Movement

A particle suspended in air is subject to uncontrolled position changes caused by molecular movement. Based on the kinetic gas theory, the length of the distance $\bar{\Lambda}$, in which a particle of radius r "in the middle" is displaced in time t, will be:

$$\bar{\Lambda} = 4.86 \cdot 10^{-6} \sqrt{\frac{t}{r}\left[1 + \frac{10^{-5}}{r}\left(0.846 + 0.290 \cdot e^{-1.25 \cdot 10^{5} \cdot r}\right)\right]} \quad (1)$$

(The formula is based on a deduction by A. Einstein[1], to which was added Millikan's formula on air current particle contents.) The definition "in the middle" means as in mathematical statistics, that the movement is less than $\bar{\Lambda}$ in 2/3 of the cases, and freater in 1/3. Next to $\bar{\Lambda}$ which gives the displacement of the particles' center, the important question is, what tube radius is necessary for a particle to travel freely through a tube and what is its expansion. The area in which a particle of radius r remains in its entirety during time t with the 2/3 possibility, is G,

$$G = \bar{\Lambda} + r \quad (2)$$

called the "middle field limit".

Figure 2 gives a simple, but still representative picture of the various good adaptations of particles of various dimensions penetrating from narrow tubes. The values G are presented here as functions of the particle-radius r at varying times t. It appears that the particle of an approximate size $r = 10^{-4}$ cm ($= 1\mu$) have the lowest G values, and therefore seem to be able to pass through narrow tubes most easily. However the important processes which will be discussed later under b) and c) are not yet being considered here.

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[1] Einstein, A: Am. Phusik 17, 549 (1905); 19, 371 (1906)

(See Figure 2)

On the basis of the Gaussian "error integral" $\bar{\Lambda}$ results in:

$$\phi(x) = \frac{2}{\sqrt{\pi}} \int_0^x e^{-x} dx \qquad (3)$$

in which the value $\phi(\Lambda) = 2/3$ is given, by the probability that a particle varies to a distance x which is smaller or larger than . For example graphically on obtains, that with a probability of 0.37 a particle is subjected to a sidplacement less than $\frac{1}{2}\Lambda$, therefore, that 37% of all particles displace themselves less than $\frac{1}{2}$ of Λ from their original location; the probability of 0.093 results in the same way from $1/8\,\Lambda$. If the particles under consideration always remained in the center of the tube (Bronchi) at the beginning, the probability of a particle deposit on the tube wall could already be given as a result of molecular displacement. It must still be assumed that the particles are located at any point in the tube cross-section, and that the distance from each particle to the tube wall is therefore different according to different directions.

A well known Theorem in analytical geometry states that the distance ρ from a particle (considering the particle center) to a tube wall is measured perpendicularly to the tube axis.

$$\rho = \left| \delta \cdot \cos\alpha \pm \sqrt{a^2 \cdot \delta^2 \cdot \sin\alpha} \right. \qquad (4)$$

where δ represents the particle distance from the tube axis (eccentricity), a the tube radius and α (which may take on values from 0 - 360°) the considered direction; if $\alpha = 0$, $\rho = a - \delta$. The anticipated probability of a particle encountering the tube wall for the distance of length ρ in a certain direction, may be established with the help of the value Λ and equation (3). A definite area aidth must be supposed. The probability (F) that the particle comes into contact with any one section of the tube wall is reached through deduction. Generally an arbitrary original particle location in the tube cross-section is assumed, as given in δ,

$$P = \frac{1}{90a^2} \int_{\delta=0}^{\delta = a - r} \delta \int_{\alpha=0}^{\alpha = 180} [1 - \phi(z)]\, d\alpha\, d\delta, \qquad (5)$$

where $z = 0.684 \frac{\rho}{\Lambda}$ or better, as the particles own should be considered, should replace it.

$$z = 0.684 \frac{\rho - r}{\Lambda} \qquad (6)$$

As the $\phi(z)$ (δ equation (3)) error-integral is not analytically solvable, equation (5) must be solved by the detailed graphic method.

The true values of the various sections of the Bronchial Trac, as given in Table 1, are to replace the tube radius a and the through stream-time t . The particle's radius r will vary according to the dimensions to be discussed.

As can easily be seen, the same values will hold true for the spherical aereols as for the cylindrical bronchi and bronchioli.

The calculations and graphic evaluations resulted in the probability values (given in per cent) listed in Table 2, for suspended particle deposits in single lung sections, as caused by the Brownian Movement. As soon as the large particle count of an aerosol is considered, the "probabilities" no longer have the significance of coincidences, but present reliable percentage rates. The table gives the particle quantity deposited in every ~~an~~ lung section, by the percentage of the total quantity which enter the particular lung section.

<u>Table 2.</u> Deposit of suspended particles in particular lung sections according to Brownian Movement (in percentage)

Lung Sections	r=0.03μ	r= 0.1μ	r=0.3μ	r= 1μ	r= 3μ	r= 10μ	r= 30μ
A	0.12	0.05	0.02	0.01	0.01	0.01	0.01
B	0.16	0.06	0.03	0.02	0.01	0.01	0.01
C	0.21	0.08	0.04	0.07	0.01	0.01	0.01
D	0.41	0.16	0.08	0.04	0.02	0.01	0.01
E	0.77	0.31	0.15	0.08	0.04	0.02	0.01
F	4.54	1.78	0.84	0.43	0.24	0.13	0.07
G	4.80	1.89	0.89	0.45	0.25	0.14	0.08
H	26.3	10.4	4.91	2.48	1.40	0.76	0.44
I	21.2	8.4	3.95	2.00	1.10	0.59	0.34

The deposits by molecular movement of small radius particles and in small areas of the lung tract, therefore a relatively greater surface, were naturally much more numerous. The molecular movement plays an unimportant role in cases of particles with a large radius.

b) Sedimentation

During penetration of the lungarea, the suspended particles are subjected to sedimentation, caused by vertical movement owing to earth acceleration, which also causes particle deposits on the walls of the bronchi and bronchioli. The depositing through sedimentation also depends on the particle fall velocity, the size of the bronchi or bronchioli, the time during which the fall continues ("through streaming time"), the direction in which the bronchi or bronchioli run paralell to the horizontals. The greater the tendency to the horizontals the less noticeable is the influence of sedimentation. The sedimentation

in all bronchi and bronchioli differs, since they (from point C on, in the Table) have varying tendencies towards the horizontals.

By applying the tendency curve ψ, the particle radius r, the through streaming time t, the tube radius (Bronchus, bronchiolus) a, and with the help of Millikan's formula quoted above, one may conclude that the probability of particle deposits in the tube is:

$$P = \frac{180-\beta}{180} + \frac{\sin\beta}{2\pi} \qquad (7)$$

therefore

$$\cos\frac{\beta}{2} = \frac{115\cdot10^{[illegible]}\cdot r^2\cdot t}{2a}\cos\psi\left[1+\frac{10^{[illegible]}}{r}\left(0.[illegible] + [illegible]\right)\right] \qquad (8)$$

It has been assumed that the particles are spherical in shape[1] and that their specific weight is 1. As P cannot be calculated singly for every bronchius and bronchiolus with its corresponding value $\cos\psi$, an average value must be entered, which may be established by:

$$\cos\psi = \frac{2}{\pi}\int_0^{\frac{\pi}{2}}\cos\psi\cdot d\psi = \frac{2}{\pi} = 0.64$$

$\cos\psi = 1$ will be entered for the Trachea (A) and the main bronchi (B); this corresponds to the dorsal length of the human body.

The probability of sedimentation in the assumed spherical alveola results as:

$$P = \frac{3}{2}\cdot\cos\frac{\beta}{2} - \frac{1}{2}\cos^3\frac{\beta}{2} \qquad (9)$$

with the value of $\cos\beta/2$ is as given in equation (8), replacing $\cos\psi = 1$; a is now the alveolae radius. The probability P for deposits through sedimentation, calculated by equations (7) and (9) are given in Table 3, in the same way as was given in Table 2 above.

Table 3. Deposits resulting from Sedimentation

Lung Sections	r=0.03	r=0.1	r=0.3	r=1	r=3	r=10	r=30
A	0.01	0.01	0.01	0.09	0.8	7.8	67.0
B	0.01	0.01	0.01	0.09	0.7	7.6	67.
C	0.01	0.01	0.01	0.05	0.45	4.5	40.7
D	0.01	0.01	0.01	0.10	0.9	9.0	73.8
E	0.01	0.01	0.03	0.27	2.2	24.8	100
F	0.01	0.06	0.39	3.6	30.8	100.	100
G	0.01	0.06	0.36	3.4	23.7	100.	100
H	0.13	0.69	4.3	40.5	100	100	100
I	0.31	1.67	10.4	84.	100	100	100

c) Effect of inertia

In all places where the stream is subjected to direction changes, the suspended particles, depending on their inertia, execute motion relative to the surrounding medium. This effect is evident at all forking points of the bronchi and bronchioli during breathing resulting, in a certain amount of particle deposits on the walls in the immediate vicinity of the forking points. The deposit depends on the particle size (radius r), the stream velocity (u), the direction change angle (ϕ) and the tube radius (a). With the aid of the Stokes formula one may evaluate the path S, covered by a particle (spherical, of specific weight 1) relative to the medium,

$$S = \int_0^{u \cdot \sin\phi} \frac{2r^2}{9\eta}\, d(u \cdot \sin\phi) = \frac{2r^2 u \cdot \sin\phi}{9\eta} \tag{10}$$

Where the constant of interval air friction is:($\eta = 1.9 \cdot 10^{-4}$ (cm^{-1} g sec^{-1}) for 37° C

The deposit probability is:

$$P = \frac{180 - \chi}{180} + \frac{\sin\chi}{2\pi} \tag{11}$$

when

$$\cos\frac{\chi}{2} = \frac{r^2 u \cdot \sin\phi}{9\eta a} \tag{12}$$

The value 30° will be given for the Turning anle at the bronchi and bronchioli forking points $A \to B$, $B \to C$ – – – – – – $F \to G$, 90° for the passage from the bronchioli respiratorii to the ductuli alveolarii G→H and 0° for the last passage into the spherical sacculi. This was fully indicated by the natural circumstance. The probabilities P, which are thus obtained from equation (110 are given in Table 4.

Table 4. Deposits through the effect of inertia

Lung Section	r = 0.3μ	r = 1μ	r = 3μ	r = 10μ
A-B	0.010	0.114	1.02	11.4
B-C	0.023	0.258	2.31	25.6
C-D	0.034	0.372	3.35	36.7
D-E	0.022	0.248	2.24	24.8
E-F	0.016	0.175	1.56	17.3
F-G	0.002	0.022	0.20	2.1
G-H	0.006	0.066	0.61	6.6
H-I	-	-	-	-
backwards				
I-H	-	-	-	-
H-G	-	-	0.01	0.1
G-F	0.001	0.011	0.10	1.2
F-E	0.001	0.006	0.06	0.6
E-D	0.004	0.039	0.36	3.9
D-C	0.008	0.091	0.84	8.9
C-B	0.009	0.101	0.89	9.8
B-A	0.007	0.081	0.72	7.9

d) Peripheral effect

A fourth occurance of deposits of particles suspended in the air, which is related to the forking points of the bronchi and bronchioli just as that discussed above, quantitatively is only of small importance, however it must be given here for the sake of completeness. It is always of importance when the particle sizes compare with the tube distances.

An area exists near the tube walls, in which the existance of a suspended particle is impossible (because of the voluminous spread of the particles); the width of this peripheral zone is equal to the particle radius. A certain number of the suspended particles must be deposited when an aerosol enters a tube, namely as many as proportionately fall into the peripheral zone. The peripheral effect depends on the proportion existing between the particle radius and the tube radius. On the supposition that the peripheral zone of a tube does not immediately change into the following, as is justified in the case of forking points in the lung, the probability for paticle disappearance at the forking points is as follows:

$$P = 2\frac{r}{a} - \left(\frac{r}{a}\right)^2 \qquad (13)$$

Table 5. Deposit caused by peripheral effect

Lung Section	r = 1 μ	r = 3 μ	r = 10 μ
A–B	0.05	0.16	0.53
B–C	0.10	0.30	1.00
C–D	0.20	0.60	2.00
D–E	0.27	0.80	2.65
E–F	0.67	2.00	6.55
F–G	0.80	2.39	7.84
G–H	2.0	5.90	19.0

The radius of the tube into which the aerosol penetrates is always to be substituted for a . The P values according to (13) are given in Table 5; they are only small.

3. Compilation of the individual data

The four seperate proceedings described in section 2, all take place simultaneously when an aerosol enters the lung, and the resulting effects, which lead to particle deposits on the walls of the lung tubes, are added togehter. Tube deposits (Trachea, main bronchi, etc) are obtained by adding the effect of molecular movement and sedimentation. Deposits at the forking points (beginning with the first bifurcation) are calculated by adding the effect of inertia and the peripheral effect. However one must be careful when using the percentages given in Table 2 and 5 that they always be 100 % particle masses at the area in question. The deposit of particles must be studied in retrogressive steps in the diminution of the particle quantity from the Trachea on, so as to obtain the true distribution of the deposited particle quantities of an inhaled aerosol in seperate lung sections; the path of the aerosol from

the trachea to the sacculi alveolari and back to the trachea must be followed.[5] Table 6 which illustrates values for specific particle sizes from 10 down through Figure 3 - 8, was reached in this manner.

<u>Table 6.</u> Total values for suspended particle deposits in % at penetration of the Trachea with given particle quantities.

Lung Section	r=0.03μ	r=0.1μ	r=0.3μ	r= 1μ	r= 3μ	r = 10μ	r = 30μ
A	0.16	0.04	0.05	0.10	0.2	7.8	67
A-B	0.01	0.01	0.02	0.16	1.2	11.0	33
B	0.21	0.10	0.05	0.11	0.7	6.2	
B-C	0.01	0.01	0.03	0.27	2.5	20.0	
C	0.28	0.13	0.07	0.07	0.4	2.5	
C-D	0.01	0.01	0.04	0.57	3.8	20.3	
D	0.55	0.26	0.13	0.14	0.8	2.9	
D-E	0.01	0.01	0.02	0.52	2.7	8.0	
E	1.03	0.51	0.29	0.35	2.0	5.3	
E-F	0.01	0.01	0.02	0.84	3.1	3.8	
F	6.1	3.1	2.0	4.0	25.4	10.2	
F-G	0.01	0.01	0.01	0.79	1.5		
G	6.3	3.2	2.0	3.7	16.0		
G-H	0.01	0.01	0.01	1.8	2.5		
H	37.2	19.1	15.8	40.3	36.6		
H-I	0.01	0.01	0.01	1.1			
I	14.1	6.6	12.7	41.6			
???	34.0	64.0	65.8	2.6			

The Table and the description show that particles with a 30μ radius or larger can hardly penetrate into the lungs because for the most part they are deposited in the Trachea (according to the of the human body explained above.) or lastly at the Bifurcation. Particles of a 10μ radius reach into the bronchioli terminales, up to the edge of the respiratory section of the lung. Most of the 3μ particles are deposited in the respiratory section, but do not reach the sacculi alveolarii, in which the 1μ particles are for the first time deposited in large quantities. 2.6 % of the 1μ particles cover the entire path from the Trachea to the sacculi and back without being deposited, because they are exhaled. The exhaled percentage increases noticeably with the smaller particles, and consists of approximately 65 % with both the 0.3μ and the 0.1μ particles. Increased deposits in the respiratory section was evident with the 0.03μ particles, the smallest to be studied here, and a resulting diminished exhaling from the lungs. Whereas heavy deposits of large particles have been noticed at the forking points, the small particles are completely absent because of their limited inertia. The effect of inertia and fall movement controls the large particles, while molecular movement acts on the small ones. Both effects are only relatively small in particles with a radius of 0.1 to 0.3μ resulting in the fact that these particles are deposited in the lung less than all others. (A smaller particle size

appears for the greatest penetration probability cobrary to Figure 2 because the question is different.)

The computing values have been determined by the 100 % particle quantity of the aerosol at the place of entrance into the Trachea. During research and obsevation of living man, in this connection the important question will be to compare the deposited particle quantities in the seperate lung sections to the particle quantity (density of the aerosol outside the human body). However this question does not differ greatly from that treated here; for, as can easily be recognized by the above data, only a limited deposit takes place with small particles in the throat and the larynx; on the other hand the large drops which deposit themselves in the throat and larynx in visible quantities, are only of little importance for lung inhalation.

In connection with the resulting value one should mention that naturally, the original simplified hypotheses, made at the beginning of the calculations, concerning the plan of the bronchial tree and the breathing process, in no way diminish the high accuracy demand of the number values (the multiple figure resutls of the number values will only offer opportunities for comparison) but on the contrary the established order of magnitude of the discussed processes will not be disproved by the results. The following should be observed: The result calculated for the 3μ particles, that absolutely no penetration and deposit occurs in the sacculi alveolarii is actually not correct; the average angle tendency of the ductuli alveolarii accepted in the calculations for sedimentation is certainly exceeded in part, so that a complete deposit of 3μ particles does not result in the ductuli and t that seperate 3μ particles penetrate the sacculi. Similar small inaccuracies may still exist at other places, in very restricted numbers. In most observations this will play no quantitative part.

4. Experimental Test

Experimental research was to show whether the data reached by the above calculations was generally in agreement with the true facts, further more it was to be established, whether actually one of the number v values reached here on the basis of previously given particle sizes has a corresponding portion in the respiratory section of the lung. An aerosol produced by ducting of a table salt solution was used during the tests; the particle sizes (which simultaneously were very different in nature) and likewise the quantity, in which various particle sizes appeared, were known on the basis of physical research. The aerosol was drawn through the lung (as fresh as possible) of a large animal (dog, calf, sheep) from the trachea to the bronchioli terminales, & which were opened by severing the pleura and the greatest part of the alveolae. The drawing through of the aerosol containing air was based on the principal of automatic lungs, only for the inhaling direction. The airstreams velocity was based on the natural ventilation velocity. The aerosol density (particle quantity pro air volume) was established before and after the passage of the aerosol containing through the lung by means of quantitative table salt analysis, through use of a glass-wool filter to catch the aerosol drops. This resulted, in the fact that a drop-volume passed through the lung, which under

consideration of the various drop-sizes of the aerosol, coincided quite pleasantly with the above given calculation data. The experiment data may thus be used as a support for the above given theory.

CONCLUSION

The area of application of the theory presented here and of its data could in the first place adapt lung inhalation to therapeutic ends. Figure 3 - 8 constitutes simple picture, showing where in the lung aerosolt particles are deposited depending on size and on the other hand allow one to seek the particle size best adapted to a controled treatment of a certain lung section, or the most appropriate inhalation haze. For example it is not hard to establish that haze with a drop radius of approximate 10µ is least suited for treatment of the bronchi, while the srop size r = 1µ is well adapted to the exclusive handling of the alveoli (the specific weight 1 is established for the liquid in this case.)

A further area of application, with one could originally only deal in theory, is the problem of lung contrast filling by inhalation for the purpose of x-ray diagnosis. The problem has been worked on experimentally by the author in close cooperation with Dr. Zeplin (previously at the Barmbeck Hospital, Hamburg); the tests have given promising results.

SUMMARY

The quantity of suspended particles of various sizes ("suspended substances") in the inhaled air which is deposited in various sections of the bronchial tree was numerically calculated on the basis of physical reflections on a lung plan adapted as closely as possible to the human lung. The data shows that larger particles (radius greater than 10µ) attach themselves to the muceous membrane in the trachea and the large bronchi, smaller ones (radius approximately 0.1µ) on the other hand are mostly filtered out in the respiratory section of the lung; even smaller particles (radius between 0.1 and 0.3µ) are exhaled for the most part, a large quantity of the smallest particles to be considered will again be deposited. The calculation results may be considered correct on the basis of experimental cross-checking. They may therefore be used for medical purposes, when it is a question of choice of the most fitting suspended particle size for inhalation treatment of a definite section of the bronchal tree.

Note: See original article for all figures.